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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,050	01/16/2001	Todd J. Friends	LA0057 NP	4974

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EXAMINER	
GUPTA, ANISH	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/761,050	FRIENDS ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 20-30* is/are rejected.

7)☒ Claim(s) *15-19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *0801*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-14, 20-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In reviewing a claim for compliance with 35 U.S.C. § 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. § 112, second paragraph by providing clear warning to others as to what constitutes infringement of the patent. See *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000). If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. § 112, second paragraph would be appropriate.

In the instant case, Claim 1 and every subsequent dependent claim thereafter recite, for variable R7, is a group "capable of bioconversion to generate the free phenol structure (wherein R7 = H)." First it is unclear what R7 is to be defined as. Applicants claims in essence are a range within a range because on hand the claims state R7 is a hydrogen, alkanoyl or an aroyl group (broader) on the other hand the claims state R7 = H (followed by a narrower limitation). Thus, it is unclear what R7 is to be defined as in the claim.

Secondly, it is unclear group qualifies as one that is "capable of bioconversion to generate a free phenol structure." It is unclear if H is that desired group or some other group. In reviewing the specification, a concise definition is not provided for this group. Thus, one of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement.

First paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 20-21, 23 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of obesity, hypercolesterolemia, arteriosclerosis, depression, osteoporosis, hypothyroidism, goiter, glaucoma, cardiac arrhythmia, congestive heart failure, and skin disorder or disease, does not reasonably provide enablement for prevention or inhibition of said diseases or prevention, treatment or inhibition of thyroid cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use , the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or

absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation

(1) The nature of the invention:

The invention is drawn to compounds that are thyroid receptor ligands which are selective for the thyroid hormone receptor β.

(3) The relative skill of those in the art

The relative skill of the those in the art is high.

(2) The state of the prior art and (4) The predictability or unpredictability of the art

It is well known in the art that for cancer therapy, while drugs are effective in vitro and in mice, are not effective in humans. For example, Dermer states that "immunotherapy's killing power of the transformation of 3T3 cells by a mutated protooncogene, simply does not have the same significance for cells in vivo.' (See page 320). Further, "[t]he facts indicate, however, that petri dish cancer is really poor representation of malignancy, with characteristics profoundly different from human disease." (See page 320). Similar sentiments are echoed in a Science article by Trisha Gura. The article indicates that the fundamental problem in cancer research is that model systems are not predictive of in-vivo activity (see page 1041). The article goes on to state xenograft models in mice "don't behave like naturally occurring tumors in humans--they don't spread to other tissues." (See page 1041). Further, other systems such as clonogenic assays are not always helpful since they "can't always predict how a tumor will respond to a drug in an animal" and "[s]ometimes they don't work because the cells simply fail to divide n culture." (See page 1042). In essence, the art indicates that

"rodents are better predictors of human reaction to cardiovascular or anti-inflammatory agents than cancer or diseases of the central nervous system." (See Time article by Frederic Golden on page 44).

(5) The breadth of the claims

The method claims are drawn prevention of the disorders claimed, inhibition of the disorders claimed and prevention, inhibition, and treatment of thyroid cancer.

(6) The amount of direction or guidance presented and (7) The presence or absence of working examples

The specification sets forth some insight treatment of the claimed disorders with appropriate dosage regiment and appropriate means of administration. However, the specification fails to provide any guidance with respect to prevention, inhibition, or treatment of thyroid cancer. The instant specification does not teach a single example, conducted either in vitro or in-vivo, that would lead one to believe that the claimed compounds are invention are effective in treating thyroid cancer. Although working examples are not necessary in the specification, lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art. Here, as indicated above in the state of the art, the treatment of cancers is fraught with problems. One can not conclude, based on even animal models, that a drug will be effective in vivo in human patients. Immunotherapy's killing power of the transformation of 3T3 cells by a mutated protooncogene, simply does not have the same significance for cells in vivo. Clonogenic assays are not always helpful since they "can't always predict how a tumor will respond to a drug in an animal" and "[s]ometimes they don't work because the cells simply fail to divide n culture." (See page 1042). In essence, the art indicates that "rodents are better predictors of human reaction to cardiovascular or anti-inflammatory agents than cancer or diseases of the central nervous system." (See Time article by Frederic Golden on page 44). Thus, given the problems associated with the

treatment of cancer, one requires more guidance then just guidance as to dosage regiment and modes of administration.

Further, the specification does not provide any guidance as to the prevention of the disorders claimed. The specification does not describe how the disorders are to be prevented. Prevention implies, that once the disorder is treated with the medication, the disorder does not reoccur. However, many of the disorders claimed do not have an effect means of prevention. For example it is well known in the art that skin disorders such as psoriasis have no means of prevention. At best, this disorder can only be controlled not prevented or inhibited. The Merck Manual states, with respect to psoriasis, that "complete preeminent remissions rare. . .No therapy assures patients of a cure.." (see page 2435). Zugerman states that Chloracne is "difficult if not impossible to treat adequately and once present, may persist for years" (abstract). For lichen planus, the Merck Manual states that the "disease tends to be self-limiting but may recur after years" (see page 2438). This indicates that a prevention is not know since recurrence persist after treatment. For Keloid, the Merck Manual states that known therapies of treatment are often ineffective and surgical or laser excision maybe necessary (see web print out). Again, the Merck Manual implies that there is no known prevention, short of excision. In glaucoma, it is known that there is a slow degeneration of the vision from slight loss to absolute blindness. Further, as the disorder progress it becomes more difficult and there is less effectiveness in preventing blindness. In such an instance, it is unclear how the disorder is to be prevented or inhibited. Given the problems associated with prevention and inhibition of disorders, more guidance is necessary. However the specification lacks the appropriate information to allow one of ordinary skill in the art to use the claimed compounds to prevent or inhibit the claimed disorders.

The Board of Appeals has held *Ex parte Sudilovsky*, that a disclosure was non-enabling since:

> "[t]he specification, though highly detailed, is devoted solely to a description of compounds stated to be known ACE inhibitors. The remainder of the specification is directed to how to make tablets and solutions for injection. Any disclosure regarding utility is confined to broad allegations and suggestions without substantiating working example. As stated in *In re Glass*, 492 F.2d 1228, 181 USPQ 31, 35 (CCPA 1974), 'the strong feeling one gets from reading the entire specification is that either appellant did not have possession of the details of a single operative process or, if he did, he chose not to divulge them.'"

Ex parte Sudilovsky, 21 U.S.P.Q2d 1702 (BPAI 1991). Similarly, the disclosure of the instant application, with regard to the prevention and inhibition, is confined to broad allegations and suggestions without substantiating working examples. When a patent applicant chooses to forego exemplification and bases utility on broad terminology and general allegations, he runs the risk that unless one with ordinary skill in the art would accept the allegations as obviously valid and correct, the examiner may, properly, ask for evidence to substantiate them. *In re Novak*, 306 F.2d 924, 134 USPQ 335 (CCPA 1962) 4; *In re Fouche*, 439 F.2d 1237, 169 USPQ 429 (CCPA 1971). In this case, Applicants specification provides ample guidance on how to make the claimed compositions. However, the specification fails on how to use the claimed compounds in that the disclosure has not provided evidence of record of a single compound that would prevent or inhibit the claimed disorders.

(8) The quantity of experimentation necessary

Since, the art indicates a level of unpredictability in treating cancer is high and the instant specification provides very little guidance on the prevention or inhibition of cancer or any other disorder, one would be burdened with undue experimentation to practice the claimed invention.

3. Claims 15-19 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The closest prior art Masukawa et a al. teach compounds that, at first sight, is seemingly similar to the claimed compounds (see col. 25, lines 1-14). However, this compounds is structurally distinct from the claimed invention since one of the phenyl groups does not have any substitution as required by the instant claims and the other phenyl group has two additional substations as compared to the claimed compounds. The prior art does not teach nor suggest any motivation to modify the phenyl groups in the manner claimed in the instant application. Accordingly, the claimed compounds are free of prior art.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback , can normally be reached on (703)306-3220. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Anish Gupta 12/9/03